

STUDY ON PREVALENCE OF PULMONARY TUBERCULOSIS IN DIABETES MELLITUS

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CERTIFICATE

This is to certify that this dissertation entitled “**STUDY ON PREVALENCE OF PULMONARY TUBERCULOSIS IN DIABETES MELLITUS**” submitted by **Dr. C. VAISHNAVI PRIYAA** appearing for Part II M.D. Branch I General Medicine Degree examination in March 2010 is a bonafide record of work done by him under my direct guidance and supervision in partial fulfillment of regulations of Tamil Nadu Dr. M.G.R. Medical University, Chennai. I forward this to Tamil Nadu Dr.M.G.R. Medical University, Chennai, Tamil Nadu, India.

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INTRODUCTION

Tuberculosis is one of the oldest diseases known to affect human. Today pulmonary tuberculosis has become the important communicable disease in the world with one-fifth of the global Tuberculosis incidence is from newly diagnosed cases within India. Approximately two million people acquire tuberculosis yearly. Of this around 45 percent will be active tuberculosis. The prevalence of tuberculosis in India according to recent WHO report is 283 per 1,00,000 population ,with 2.83 percent being MDR-TB , ie., multi drug resistant tuberculosis. In spite of availability of effective treatment the annual deaths due to tuberculosis in India is 3,31,000.

Tuberculosis flourishes where poverty malnutrition overcrowding and lack of adequate medical care are seen. Diabetes mellitus, alcoholism, malnutrition, chronic lung disease and any debilitating or immunosuppressive conditions are considered to enhance the chances of contracting this dreaded disease.

TUBERCULOSIS IN DIABETES:

Tuberculosis is a single infectious disease that involves multiple endocrine organs namely adrenal cortex anterior and posterior pituitary and parathyroid gland. It doesn't directly involve insulin secretion of beta cells

of pancreas but worsens the metabolic control in diabetes.

Some antituberculous drugs produce problems in management of diabetes .On the other hand Diabetes mellitus aggravates the existing tuberculous infection and also activates silent or dormant tuberculous focus in the body.

Vicenna (980- 1027 A.D) is said to have been the first to note the frequent association of Diabetes and tuberculosis.¹ It is greatly agreed that pulmonary tuberculosis develops early in untreated diabetes , and once present ,progression is rapid unless both the conditions are treated .Wilson Fox (1981), found that tuberculosis commonly appeared diabetes has been lasted for 1-2 year.

The link between diabetes mellitus and pulmonary tuberculosis has been talked of at various fora, but has never occupied the central stages of discussion. There is a growing amount of evidence of one disease fuelling the other. The interest in diabetes and tuberculosis is mounting rapidly and it promises to be an exciting time for researchers and clinician involved in the study of dual diseases.

Also the clinical and radiological manifestations of tuberculosis is varying among diabetes and non diabetes population. There are numerous

issues of basic, applied and operational research waiting for solution. It is a wake up care for all clinicians and researchers to gear up to meet the challenge of the brewing double trouble. Hence an attempt has been made to study the dual issue among native South Indian population to confirm or refute the published observation.

AIM OF THE STUDY

1. To screen diabetics for pulmonary tuberculosis and find out the prevalence of tuberculosis in diabetic patients.
2. To estimate the age groups and sex ratio in diabetic patients with tuberculosis.
3. To study and compare clinical symptoms and signs of tuberculosis associated with diabetes.
4. To assess the various patterns of radiological findings in tuberculosis in association with diabetes.
5. To correlate the smoking habits with reference to prevalence of tuberculosis in diabetic and non diabetic population.

REVIEW OF LITERATURE

DIABETES MELLITUS- TUBERCULOSIS:

The link between diabetes mellitus and pulmonary tuberculosis has been talked of at various fora but has never occupied the centre – stage of discussions. Presently, an epidemic of diabetes is on both in developed and developing nations. With the recognition of this explosive, increase in the number of people diagnosed with diabetes mellitus all over the world, a whole new field of issues related to interaction between diabetes and pulmonary tuberculosis has been thrown open.

The global figure of people with diabetes is projected to rise from the current estimate of 150 million to 220 million in 2010 and 300 million in 2025 most cases will be of type -2 diabetes, which is characterized by insulin resistance and or abnormal insulin secretion .people with type-2 diabetes are not dependent on exogenous insulin, but may require it for control of blood glucose levels if this is not achieved with diet alone or with oral hypoglycaemic agents.

The diabetic epidemic, although apparent across the world, has been most pronounced in non-European populations, as evidenced by studies in

the native American and Canadian communities, Pacific and Indian Ocean island populations, groups in India and Australian Aboriginal communities. The potential for increase in the number of cases of diabetes is greatest in Asia. Type-2 diabetes in children, teenagers, and adolescents is a serious new aspect to the epidemic and is an emerging public health problem of significant proportions.

Based on compilation of studies from different parts of the globe, the World Health Organization has projected that the maximum increase in diabetes would occur in India. Considering the large population and the high prevalence of diabetes could be enormous. With an estimated 23 million today and the numbers set to increase to 57 million by 2025, the increasing prevalence of diabetics reflects the sedentary life-style, excessive energy intake, reduced physical activity and obesity.

Studies conducted in India in the last decade have highlighted that not only is the prevalence of type-2 diabetes high, but also that it is increasing rapidly in the urban population. Of particular interest are the results of the three diabetic surveys conducted in Chennai in 1989, 1995 and 2000. They show a rising trend for diabetes mellitus and glucose intolerance. The period between 1989 and 1995 shows a 40% rise in the prevalence. A nation-wide study conducted in six major cities in India in the year 2000 showed that the

prevalence of diabetes in urban adults aged more than 20 years was 12.1%. Onset of diabetes occurs at younger age in Indians.

The prevalence of impaired glucose tolerance test, which is a forerunner of diabetes, is also increasing especially among the younger population. There is also a wide urban-rural difference in the prevalence of diabetes pointing to the major role urbanization may be playing in the causation of the disease.

Patients with diabetes mellitus are also at a higher risk of tuberculosis. This has been highlighted by several retrospective and prospective studies. In a study in Mumbai, tuberculosis was found to be the most common complicating illness (5.9%) in a large cohort of over 8000 patients with diabetes mellitus³. In a recent study from the Regional Institute of Medical Science, Imphal, the prevalence of pulmonary tuberculosis in diabetics was found to be 27% by radiological diagnosis and 6% by sputum positivity⁴. A rising prevalence of tuberculosis in diabetes has been seen with age. Mortality rates in these patients are reported to be several times higher than in non-diabetic pulmonary tuberculosis patients. Although the relative risk of developing pulmonary tuberculosis and mortality is several times higher in patients with diabetes mellitus than in matched controls, the clinical symptoms and pulmonary tuberculosis are believed to be similar in patients with or without diabetes mellitus. And so more the bacteriological

conversion rates, and relapse rates. However, those with diabetes mellitus may relapse more often with resistant strains. In a recently published study from Congo diabetes appeared to have an induction and aggravating effect on tuberculosis. Tuberculosis was found to be more frequent in diabetics, had more pronounced radiological signs, treatment failures and deaths were also more frequent.

Do patients with tuberculosis too have a higher prevalence of diabetes mellitus? There is not enough evidence to give a definitive answer, but there are some trends. Studies conducted after the introduction of the glucose tolerance test in 1950s, have shown high prevalence of impaired glucose tolerance test in patients with tuberculosis with rates ranging from 2 to 41%. The use of different criteria for diagnosis of diabetes mellitus makes comparisons between the results of the studies almost impossible there have been reports of high prevalence rates of diabetes in cases of pulmonary tuberculosis (4-20%) and rates are higher for impaired glucose tolerance test (16-29%). After anti-tuberculosis therapy, 50% of them had normalization of glucose intolerance. Some investigators have reported an association between severity of tuberculosis and abnormal glucose tolerance. However, no association has been found with age, family history of tuberculosis, ethnicity or duration of treatment.

The cause(s) of increased susceptibility are not yet clearly understood. Some believe it to be due to the lowered production of interleukin -1B and tumor necrosis factor- α by peripheral blood monocytes in patients with tuberculosis and co- existent diabetes mellitus. Or is it the non –enzymatic glycosylation of tissue proteins inducing an alteration in connective tissue in diabetes mellitus diabetic autonomic neuropathy leading to abnormal basal airway tone due to an alteration in vagal pathways and thus cause a reduced bronchial reactivity and bronchodilatation is also considered as one of the probable causes.

Irrespective of the triggering mechanism(s), the fact remains that an epidemic of diabetes mellitus is sweeping the country .the recent prevalence data has propelled the estimates for India upwards -32m in 2000and 80m in 2030. India is also the home to the largest number of tuberculosis patients in any one country. And there is a growing amount of evidence of one disease fueling the other. The interest in diabetes and tuberculosis is mounting rapidly and it promises to be an exciting time for researchers and clinicians involved in the study of dual diseases. There are numerous issues of basic, applied and operational research waiting for solutions.

It is a wake–up call for clinicians and researchers to gear-up to meet the challenge of the brewing double trouble.

DIABETES & TUBERCULOSIS: A DANGEROUS LIAISON

Diabetes mellitus is becoming a global epidemic and India, in particular, is noted as hosting a high proportion of this disease burden. There are approximately 41 million prevalent cases of DM in India and as per the International Diabetes Federation (IDF) ESTIMATES BY 2025 this will rise to about 70 million, the largest number for any country¹.

As well as nationally predicted rises in DM rates, regional studies have also shown increasing rates of disease, with the largest reported increases in low and middle income countries occurring amongst urban population².surveys conducted in Chennai ,India , in 1989 and subsequently in 1995 showed a 40 per cent rise in the prevalence of diabetes over this period³. However India not only faces the public health difficulties associated with newly increasing rates of chronic diseases such as DM ,but as with other low and middle income countries, endures sustained rates of infectious diseases (such as TB) which remain to be brought under control.

One –fifth of the global TB incidence is from newly diagnosed cases within India; approximately 2 million people acquire TB yearly. Around 45 per cent of these incident cases will be infectious to others, further increasing the high TB disease rates⁴. It is estimated that annually around 3,31,000 people in India die form TB⁵. The recent WHO report indicates

that the prevalence of tuberculosis in India is 283 per 100,000 population with approximately 2.8 per cent of prevalent cases being problematic multi drug resistant (MDR) TB⁵. It should however be noted that although TB rates are high in India, by 2006 directly observed treatment short –course (DOTS) was being provided nationally. In India, case detection is estimated to have increased from below 20 per cent up to 67 per cent as DOTS was set up throughout all 30 districts⁴.

Rather than just existing alongside each other as diseases of high burden, TB and DM are thought to be associated with one another. Each disease is thought to be able to exacerbate the other and when an individual presents with both diseases concomitantly disease outcomes may be poorer.

Reports on the association between DM and TB are found as far back as 1000 A.D. when Avicenna noted that “phthisis”, (a Greek term for tuberculosis), often complicated diabetes and that the presence of diabetes resulted in an increased risk of developing TB⁶.

However, recently it has gone unmentioned in many global TB guidelines and in the most recent national guidelines has only been mentioned as something needing more research^{5,7}. If not acknowledged and dealt with appropriately, the association could pose a threat both to successful TB control and DM treatment.

Diabetes as a risk factor for TB:

Patients with diabetes mellitus have been found to have a higher than average risk of contracting tuberculosis. A study carried out at the regional Institute of medical sciences, Imphal found the prevalence of pulmonary tuberculosis in people with diabetes to be 27 per cent by radiological diagnosis and six percent by sputum positivity⁸.

In a study in Mumbai, tuberculosis was found to be the most commonly occurring concomitant illness in diabetics with 5.9 percent of the individuals in a cohort of over 8000 being co- morbidly affected⁹.

A meta – analysis demonstrated that having diabetes was associated with overall risk (Relative Risk) of 3.11 percent for contracting tuberculosis¹⁰. A systematic review¹¹ reporting on the association found 9 studies in which diabetes was estimated to increase risk of infection from 1.5 to 7.8 fold¹¹.

Gender seems to have no bearing upon this relationship, however the relative risk for contracting tuberculosis among individuals with diabetes does vary by age, being highest in younger groups¹¹.

In order to illustrate the potential public health importance of diabetes as a risk factor for tuberculosis, Stevenson et al, ¹¹ estimated the population

attributable risk (PAR), for tuberculosis from diabetes in India. They calculated that diabetes could account for approximately 14.8 percent of sputum positive cases¹². This calculation highlights the impact the diabetes epidemic could have upon TB rates in India, perhaps active case finding amongst people with diabetes will become appropriate in order to help control tuberculosis.

TUBERCULOSIS AS A RISK FACTOR FOR DIABETES:

The majority of studies identify and discuss the presence of diabetes as a risk factor for tuberculosis, but could the relationship between tuberculosis and diabetes be bi-directional? Engel Bach¹³ and Nichols¹⁴ posited that not only could having diabetes increase an individual's likelihood of developing tuberculosis but that having TB could lead to the presentation of diabetes. Studies have also shown both a high prevalence of diabetes and of impaired glucose tolerance (IGT), in patients with tuberculosis¹⁵. However, it is not often known if diabetes or IGT were present prior to the TB infection as high as a high proportion of people with diabetes and especially IGT are unaware of their status.

Some studies have noted a normalization of glucose levels after Tuberculosis treatment in individuals who had developed hyperglycemia.

This poses a question as to whether it is the active disease or the treatment for it causes these metabolic abnormalities¹⁶.

It is known that tuberculosis, as with other infections, complicates diabetes management, and some of the TB treatment, regimes which includes isoniazid or rifampicin have hyperglycemic effects.

POSSIBLE CASUAL PATHWAYS FOR THE ASSOCIATIONS:

Diabetes is known to cause immune dysfunction and moderate suppression of the immune system ¹⁹. Specifically, diabetes has been shown to suppress cell mediated immunity. Diabetes has been associated with a decrease in levels of leucocytes and polymorph nuclear neutrophils.

A reduced T helper (Th 1) cytokine response level is also seen amongst diabetic individuals^{19,20}. This immune dysfunction is detrimental to the immune response against tuberculosis. Th 1 cytokines are vital in control and inhibition of *Mycobacterium tuberculosis* bacilli. For example, interferon gamma, is important for combating microbial infections and both Interferon- gamma and Tumor necrosis factor- alpha, activate macrophages^{19,20}. Activated macrophages release active oxygen species (ROS), and free radicals such as nitric oxide which are essential for control of infection such as nitric oxide which are essential for control of infection,

including tuberculosis. Not only are macrophages release reactive oxygen species (ROS) and free radicals such nitric oxide which are essential for the control of infection, including tuberculosis²¹. Not only are macrophages the primary site of infection but these cells also instigate the main immune response to tuberculosis²².

Macrophage function is found to be inhibited in individuals with diabetes, with production of ROS, and phagocytic and chemo tactic functions being impaired. All of these immune processes are important for tuberculosis clearance and as such, diminution of these give a very plausible pathway for the increased relative risk of tuberculosis seen among individuals with diabetes^{19,20}.

Macrophage function has also been some plausible mechanisms highlighted in the literature through which tuberculosis infection could cause hyperglycemia .For example, aspects of the inflammatory immune response to tuberculosis infection could lead to an increase in insulin resistance for a decrease in insulin production resulting in an increase in blood glucose²².

EFFECTS OF CO-MORBIDITY ON DISEASE OUTCOMES:

As would be anticipated, given the above considerations, co-morbidity with tuberculosis and diabetes is associated with deterioration in both the conditions. A higher mortality rate for tuberculosis when complicated with diabetes has been reported.(23,24). Co-presentation related of tuberculosis and diabetes is associated with increased diabetes related complications and poorer blood glucose control. Conversely, tight blood sugar control is thought to reduce the risk of tuberculosis infection in individuals with diabetes. Concomitant TB and DM is associated with more severe features of TB including increased involvement of lower lung fields, and longer periods of smear positivity^{25,26}.

A study carried out in Nijmegen showed that individuals presenting with concomitant DM and TB, are more likely to have positive results after six months of TB treatment.²⁷. This may be because, bacterial clearance takes a longer time in diabetic patients or that bacterial load is initially higher and thus takes longer to diminish. A study carried out in Texas border population found that multi-drug resistant TB (MDR-TB), was associated with DM with an odds ratio of 2.1²⁷, while other studies show no increased association between DM and MDR-TB^{29,30}.

Nijland et al²⁸, reported that rifampicin was not absorbed effectively in TB-DM patients; this could be due to poor gastrointestinal uptake, or due to differences in metabolism, excretion and bodyweight³¹.

However in India evaluations of the category I treatment regimen (not recommended for all smear positive cases) of the Revised National Tuberculosis Control Programme (RNTCP) have suggested that it is appropriate for people with concomitant diabetes^{32,33}.

It is generally accepted that Tuberculosis is more prevalent among the diabetes than non diabetes. The reported prevalence rate varies. As far as back as 600 AD the association of these two diseases as noted by Saruthy; Avicenna was reported to have noted this association more than thousand years ago.

The relationship between diabetes and tuberculosis date back to Roman times. Autopsies in the 18th and 19th centuries were happening this association. Although the preparude bacillus was not discussed until 1882.

Presently an epidemics of diabetes is on both in developed and developing nations. With the recognition of this explosive increase in the number of people diagnosed with diabetes mellitus all over the world a

whole new field of issues record to inter action between diabetes and Pulmonary Tuberculosis has been thrown open.

The ponal figure of people with diabetes in projected to rise from the correct estimate of 150 million 220 million in 2010 and 300 million in 2015 most cases of diabetes will two type of diabetes, which is charecterised by insulin resistance and / or abnormal insulin secretion. People with type two diabetes are not dependant on exogenous insulin but may require it for control of blood glucose levels if this was not achieved with diet alone or with oral hypoglycemic agents.

The diabetic epidemic although apparent among the world has been most pronounced in Non-European population as evidenced by Smalies in the native American and Canadian Communities, Pacific and Indian Ocean Island populations, groups in India and Australian Aboriginal communities. The potential for inverse in number of cases of diabetes is greatest in Asia. Type two diabetes in children, adolescents and teenagers is serious new aspect to the epidemic and is an emerging public problem of significant proportion.

Bases of complication of studies from different parts of Globe The World Health Organisation has projected that increase in diabetes would

occur in India. Considering the large population and high prevalence of diabetes, the burden of diabetes could be enormous. With an estimation 23 million today, the number set to increase to 57 million by 2025, the increasing prevalence of diabetes reflects the sedentary life style excessive energy intake, reduced physical activity and obesity. Studies conducted in India last decade have highlighted that not only the prevalence of type two diabetes but also that it is increasing rapidly in the urban population. Of particular interest are results of three diabetic surveys conducted in Chennai in 1989, 1995 and 2000. They show a rising trend for diabetes and glucose intolerance. The period between 1989 and 1995 shows a 40 per cent rise in the prevalence.

A nationwide studies conducted in six major cities in the year 2000 showed the prevalence of diabetes in urban adults aged more than 20 years was 12.1 per cent. Onset of diabetes occurs at younger age in Indians. The prevalence of impaired glucose tolerance test which is a fore runner of diabetes is also increasing, especially among the younger population. There is also a wide urban-rural difference in the prevalence of diabetes pointing to the major role in urbanization may be playing in the causation of these diseases.

It is generally accepted that in pulmonary tuberculosis is more

prevalent among diabetics than in non-diabetics. The reported prevalence of tuberculosis rate varies. The increasing TB morbidity among diabetics has strongly been substantiated by studies of the incidence of correlation. These statistical analysis have been made either on DIABETIC PATIENTS material being taken from the case histories, in the medical wards and special diabetic hospitals and in diabetic out patient clinics or on autopsy findings and tuberculosis notification.

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RELATED STUDIES

1. Progressive age related changes in pulmonary tuberculosis images and effect of diabetes. Perz Guzman et al., Int. J. Tuberc. Lung disease 2001 May, 5 (5), 455-61. Atypical radiological images of pulmonary tuberculosis and elderly and diabetics. In diabetics a high frequency of lower lung lesions and cavitations are observed in all age groups.
2. Tuberculosis and diabetes D.C Lahiri and P.K.Sen (From B.C.Roy Research Institute , Calcutta) Indian. J. of Tuberculosis. Vol. x, xi, No.2 1974. The prevalence of diabetes is 6.5% in pulmonary tuberculosis.
3. Pulmonary tuberculosis and diabetes P.A.Deshmukh and T.Shah Ind. J. of TB.,1984.,31-114.
4. The incidence of tuberculosis in diabetes was 5.6%. Routine post breakfast blood glucose estimation should be done in all pulmonary tuberculosis patients to find out association of tuberculosis.
5. Diabetes mellitus and pulmonary tuberculosis .S. R. Tripathy et al ., Ind. J. TB 1984, 31, 122 the prevalence of tuberculosis is 4.1 % of known diabetic patients.

6. Diabetes and Tuberculosis – The brewing double trouble by Lalit Kunt
Ind. J. Tub. Vol 50. , No.4. ,Oct 2003. Tuberculosis was found to be more frequent in diabetes and more pronounced.
7. Diabetes and tuberculosis : a dangerous liaison & no white tiger Indian
J. of .TB., Res 130 , July 2009 , pp1-4 People with diabetes may be important targets for interventions such as active case finding and treatment of latent tuberculosis.

MATERIALS AND METHODS

SETTINGS : Diabetology department and Tuberculosis clinic.

STUDY DESIGN : Prospective analytical study.

PLACE : Govt. Kilpauk Medical College&Hospital, Chennai

DURATION OF STUDY : October 2008 to June 2009

MATERIALS : Five hundred cases of established Diabetes mellitus who attended the diabetology department were screened for prevalence of tuberculosis.

INCLUSION CRITERIA: [STUDY GROUP]

1. Patients with Type 2 diabetes mellitus with respiratory symptoms
2. Age group 19 to 75 years
3. Both sexes
4. Duration of diabetes was from newly diagnosed to maximum 25 years

CONTROL GROUP: Hundred patients with tuberculosis alone and not with Diabetes selected randomly from tuberculosis clinic.

EXCLUSION CRITERIA:

1. Patients treated earlier for tuberculosis
2. Immunosuppressed states
 - (i) HIV positivity
 - (ii) Steroid therapy
 - (iii) Chronic renal failure

CONSENT : Informed consent was obtained was obtained from all patients who were included in the study.

ETHICAL CLEARENCE:

Project was approved by the ethical committee Govt. Kilpauk medical college.

METHODS:

Five hundred cases of diabetes mellitus patients were screened for tuberculosis based on inclusion criteria and exclusion criteria. Prevalence was found to be 56 cases of tuberculosis among the five hundred diabetic patients. Hundred cases of patients with tuberculosis alone and without diabetes alone were taken as controls.

All patients in this study as well as control group underwent full clinical evaluation .Clinical history and physical examination findings were recorded with particular attention to Age , Sex, BMI , Symptoms and Clinical features of tuberculosis.

SYMPTOMS: Of duration 2 weeks to six months. Cases underwent the investigations for confirming the diagnosis of tuberculosis.

1. Cough with expectoration
2. Fever
3. Loss of weight
4. Loss of appetite
5. Loss of weight
6. Haemoptysis
7. Breathlessness
8. Chest pain
9. Others

PHYSICAL EXAMINATION:

All patients with established diabetes underwent thorough physical examination both General and Systemic examination.

LAB INVESTIGATIONS:

BLOOD

1. Total Wbc count
2. Differential count
3. Erythrocyte sedimentation rate

4. Haemoglobin
5. Blood sugar: Fasting (overnight) and Potprandial
6. Blood Urea
7. Serum Creatinine
8. Fasting Lipid profile

URINE:

1. Albumin, sugar and deposits.

MANTOUX:

PPD RT 23 of 1 Tuberculin unit was used.

CHEST X RAY:

Mass Miniature Radiography / Large X Ray

SPUTUM FOR ACID FAST BACILLI:

1. Sample A
2. Sample B

OTHERS: CT Chest

X ray chest radiological lesions were analysed by number of zones involved, nature of lesions like infiltration, consolidation, fibrosis, cavity and consolidation etc.

STASTICAL ANLYSIS:

Datas were entered in a Microsoft Excel computers read sheet and analysed by using WHO epidemiological information package.

SUGGESTIONS

It is worth remembering that early diagnosis of this combination of DM and TB is not that easy.

When a combination of DM and TB is diagnosed , the TB disease is already in advance stage that it makes management more difficult ,and clinical outcome is poor.

From this study the following suggestions were made.

The only way to recognize this dreadful combination is

- | | |
|-------------------------------------|--|
| 1. X ray examination | (i) Once in a year or
(ii) with excess weight loss |
| 2.X ray with Sputum AFB examination | (i) for patients with cough
with expectoration more
than two weeks |

STUDY RESULTS AND DISCUSSION

The study group comprised of 500 subjects who had established diabetes mellitus taking treatment as patients in Dr.Ambedkar institute of diabetes, Govt. Kilpauk Medical College. Out of 500 subjects 56 patients [TB DM] group were found to be suffering from also pulmonary tuberculosis. 56 age matched patients suffering from tuberculosis alone and non diabetics selected randomly were compared with DIABETIC TB GROUP [DM-TB] for age wise break up , and sex distribution, clinical symptoms and various patterns of radiological lesions and number of zones involved.

1. AGE AND SEX DISTRIBUTION

TO COMPARE THE AGE GROUP IN YEARS, AND SEX DISTRIBUTION FOR THE STUDY, SUBJECT WITH COMBINATION OF DIABETES WITH PULMONARY.

TUBERCULOSIS AGAINST TUBERCULOSIS ALONE

TB-DM GROUP [n= 56]

NON DM-TB GROUP [n= 56]

TABLE - 1

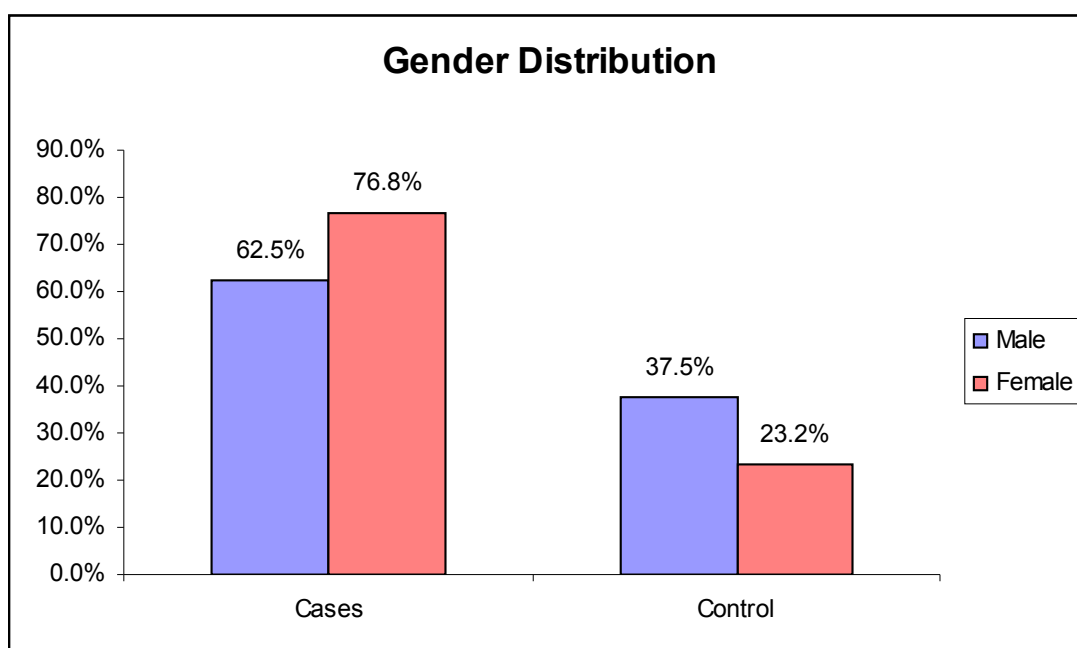
	DM-TB	NON DM- TB
No. of subjects	56	56
Male	35	43
Female	21	13
Male: Female ratio	1.67	3.31

	Male	Female
DM-TB	62.5%	37.5%
NON DM- TB	76.8%	23.2%

INFERENCE

- i) Out of 56 cases in our TB-DM, 35 were male and 21 were females.
- ii) In out of 56 NON DM-TB population, there were 43 males and 13 females.
- iii) Thus sex, male : female ratio was found to be 1. 67 in DM-TB GROUP and 3..31 for NON DM-TB GROUP. This shows a male preponderance in DM-TB GROUP, THAN NON DM-TB group

1. Tripathy et al., [1984] found the male: female ratio of 4:1 in patients having pulmonary tuberculosis with diabetes.
2. It is made out that males are more susceptible than females for pulmonary tuberculosis associated with diabetes. ICMR [Anon 1958] conducted a national survey and presented its salient findings.
3. Regarding sex Deshmukh, [1979] has listed a large number of causes grouped under occupation. The occupational hazard involved as silicosis of lungs involved in hard coal mining, textile industry containing sucking thread of bobbin, proximity to patients, socio economic level characterized by hard work and poor nutrition. This information lends support to the present findings, even though studies were not made out with a particular objective of combination of diabetes and pulmonary tuberculosis.

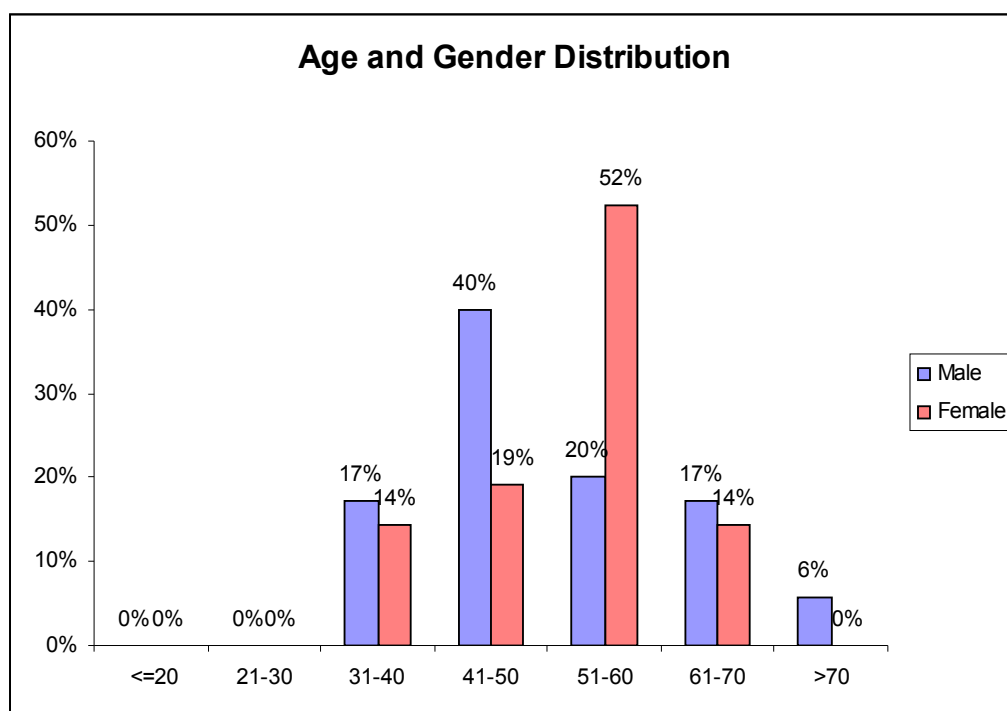


2. AGE GROUP AND SEX BREAK UP OF TB-DM CASES.

[N=56]

Table 1A

Age Group In years	Male		Female		Total
<=20	0	0%	0	0%	0
21-30	0	0%	0	0%	0
31-40	6	17%	3	14%	9
41-50	14	40%	4	19%	18
51-60	7	20%	11	52%	18
61-70	6	17%	3	14%	9
>70	2	6%	0	0%	2
Total	35	100%	21	100%	56



Chi-Square Tests

	Value	df	P-value
Pearson Chi-Square	7.407	4	.116
N of Valid Cases	56		

INFERENCE

In the DM -TB group of 56 patients majority were above 40 years of age

- i) In below 20 years group 0 cases were seen
- ii) In 21 to 30 years group 0 cases were seen
- iii) Above 40 years of age, 47 cases were found.
- iv) In 41 -50 years group, 14 cases were present
- v) In 51 to 60 years age group, 18 cases were found.
- vi) In 61 - 70 years age group, 9 cases were found
- vii) Maximum cases were found between 41 to 50 years

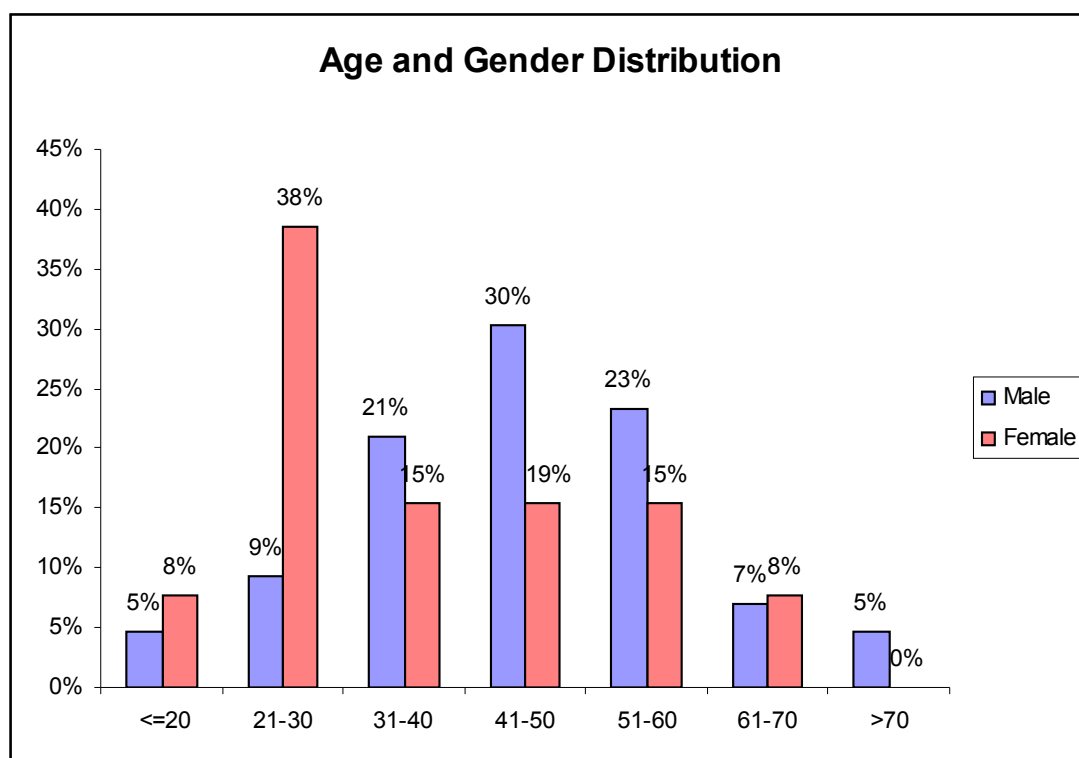
viii) 45 cases were found between 31 to 60 years of age

3. AGE WISE BREAK UP OF

NON DM-TB GROUP

TABLE -1 B

Age Group In years	Male		Female		Total
<=20	2	5%	1	8%	3
21-30	4	9%	5	38%	9
31-40	9	21%	2	15%	11
41-50	13	30%	2	15%	15
51-60	10	23%	2	15%	12
61-70	3	7%	1	8%	4
>70	2	5%	0	0%	2
Total	43	100%	13	100%	56



Chi-Square Tests

	Value	df	P-value
Pearson Chi-Square	7.332	6	.291
N of Valid Cases	56		

Chi-Square Tests

	Value	df	P-value
Pearson Chi-Square	2.703	1	.100
N of Valid Cases	112		

INFERENCE

In the NON DM-TB group,

- i) In the NON DM -TB group of 56 patients majority were above 30 years of age
- ii) In below 20 years group 3 cases were seen
- iii) In 21 to 30 years group, 4 cases were seen
- iv) Above 40 years of age, 33 cases were found
- v) In 41 -50 years group, 15 cases were present
- vi) In 51 to 60 years age , there were 18 cases
- vii) In 61 - 70 years age group , there were 9 cases
- viii) Maximum cases were between 41 to 50 years
- ix) 38 cases were found between 31 to 60 years
- x) Other groups show a more uniform pattern of distribution.

INFERENCE

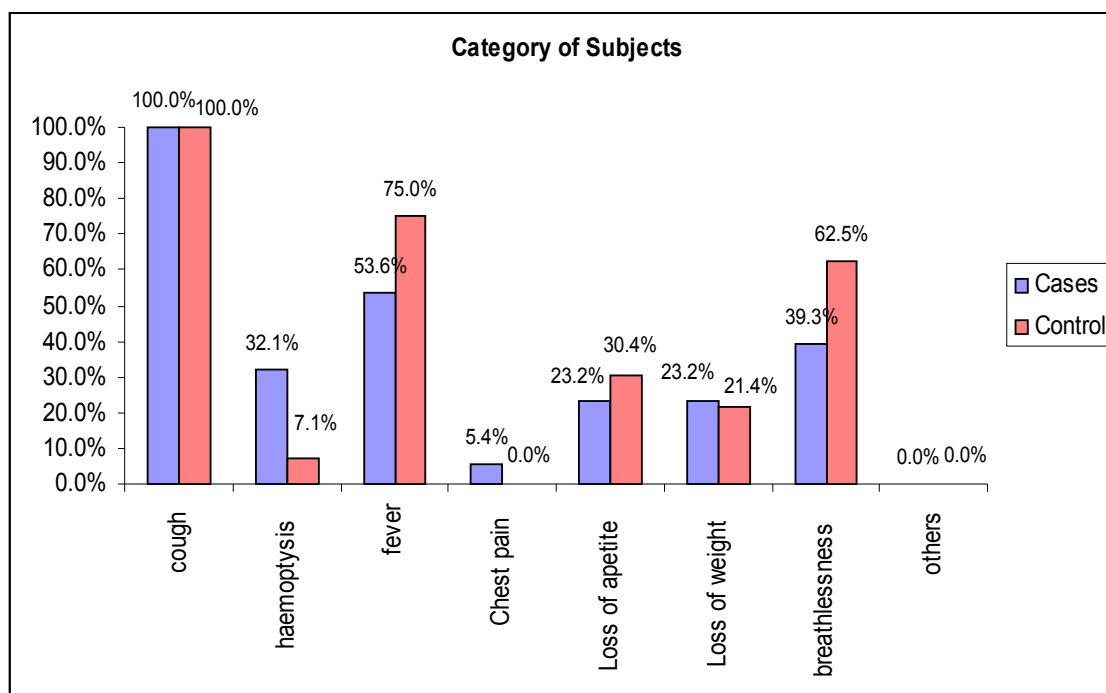
- i. Maximum patients were found in 31 to 40 years and 41 to 50 years age group.
- ii. Presence of cases distributed among all age groups in NON DM-TB group is a differentiating picture in the study.

4. SYMPTOMATOLOGY:

In terms of symptomatology the subjects suffering from tuberculosis alone and with diabetes and pulmonary tuberculosis were considered, the break up of symptoms presented in the table.

TABLE DEPICTING SYMPTOMWISE BREAK UP OF CASES

TABLE - 4A



The DM-TB group was analysed for spectrum of symptoms and majority of the patients presented with

1. Cough with expectoration 100 %
2. Haemoptysis 32.1%
3. Fever 53.6%
4. Chest pain 5.45%
5. Loss of weight & appetite 23.2%
6. breathlessness 39.3%
7. others 0%

INFERENCE

The NON DM –TB group was analyzed for the symptomatology and majority of the patients presented with,

1. fever	72%
2. breathlessness	62.5%

Clinical symptoms were seen to be almost similar in both DM-TB and NON DM-TB group. There was no significant difference in the overall symptomatology.

1. This was similar to a study conducted in Regional Institute of Medical sciences, Imphal [2, the prevalence of TB in diabetics was 27% by radiological diagnosis and 6% by sputum positivity. But the clinical symptoms and presentation of pulmonary tuberculosis was found to be similar in patients with or without diabetes.

Ref: Indian. J. of Med Res., 130 July 2009, pp 1-4.

2. Also similar study in Pakistan in 2006, shows similar findings with regards to symptomatology. “ Though the presenting symptoms of PTB does not seem to modified with DM, yet DM , can affect the radiological findings.

Ref: 1. ANNALS vol. 15 NO.2 APR-JUN 2009 , QUAZI et al

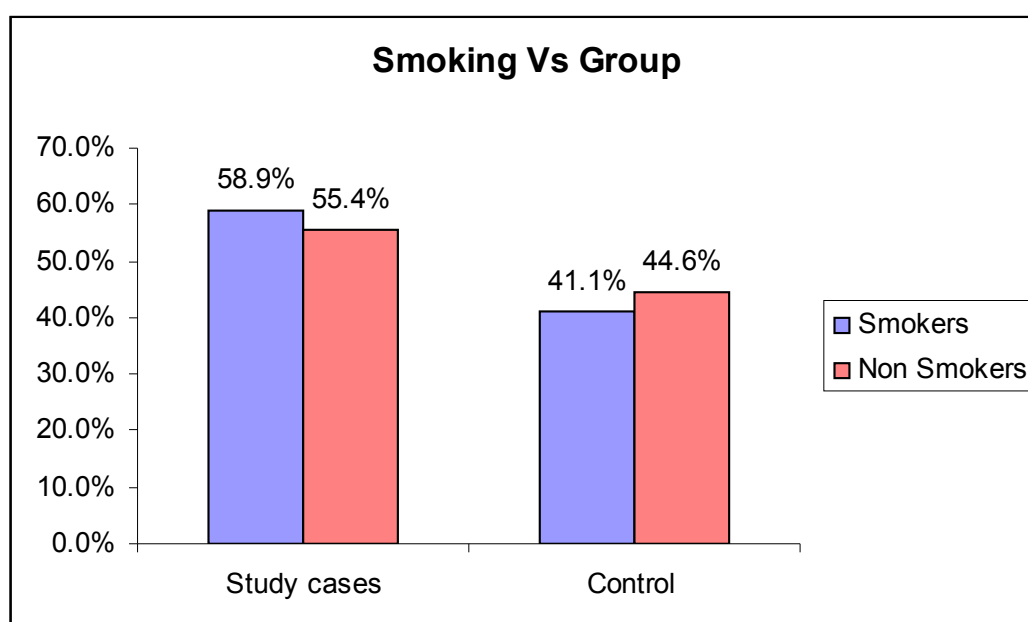
The other two studies showing no significance between symptomatology in DM and NON DM-TB are

2. Kossii et al., Pulmonary tuberculosis in diabetics. Respiration.
3. Perez Guzman C et al., Ind .J of Tub. Lung Dis. Apr 2003.

6. SMOKING HABITS AMONG MALES

TABLE - 5

Smoking among Males	DM-TB GROUP		NON DM-TB GROUP	
	No.	%	No.	%
Yes	33	58.9%	31	55.4%
No	23	41.1%	25	44.6%



Chi-Square Tests

	Value	df	P-value
Pearson Chi-Square	.146	1	.703
N of Valid Cases	112		

INFERENCE

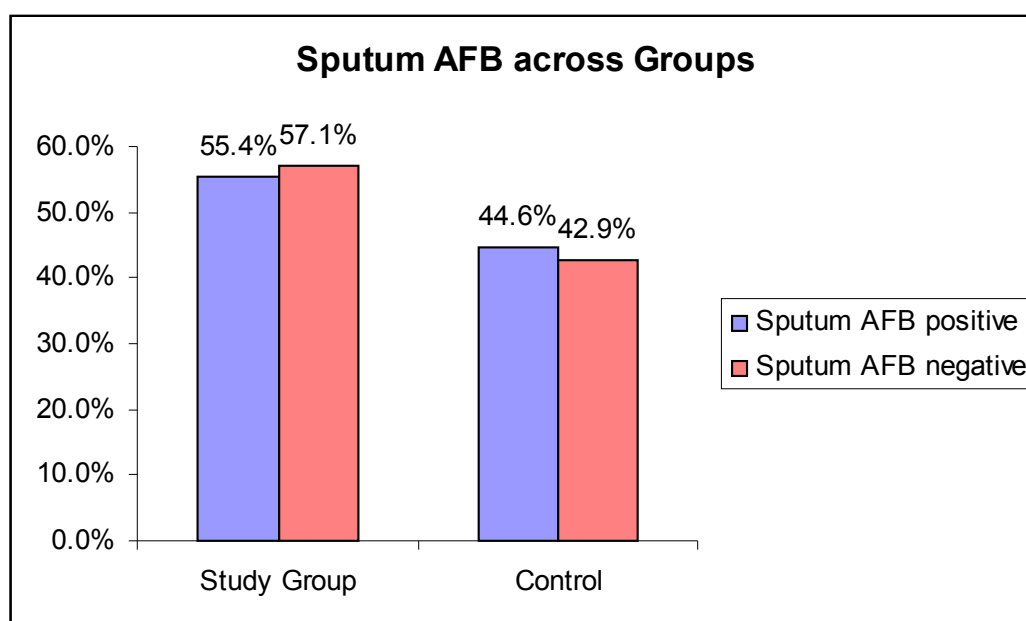
The prevalence of smoking among TB in both DM and NON-DM were 58. % and 55.4%.

This shows that smokers are more prone to develop tuberculosis than non smokers. Though there was no statistical significant correlation between DM and NON DM-TB, diabetes adds to the increased susceptibility for TB among smokers than, non smokers and NON DM group.

7. TABLE DEPICTING OCCURRENCE OF SPUTUM AFB POSITIVITY AMONG TB-DM AND NON DM-TB GROUP

TABLE – 6

Groups	Sputum AFB positive	Sputum AFB negative
DM-TB group	55.4%	44.6%
NON DM-TB group	57.1%	42.9%



Chi-Square Tests

	Value	df	P-value
Pearson Chi-Square	.036	1	.849
N of Valid Cases	112		

Of the 500 DM patients, 31 case [55.4 %] were found to be sputum positive for Acid Fast Bacilli.

In NON DM –TB group 25 case [44.6%] were found to sputum positive.

The P value was 0.849 [$p>0.05$] and hence there was no statistical significance of difference of sputum positivity between the two groups.

Hence both diabetics and non diabetic TB group showed similar sputum positivity rates, although it was slightly higher in the DM –TB group, this may be attributed to the more severe type of presentation in DM, increased mortality patterns in DM and also to delayed sputum conversion rates.

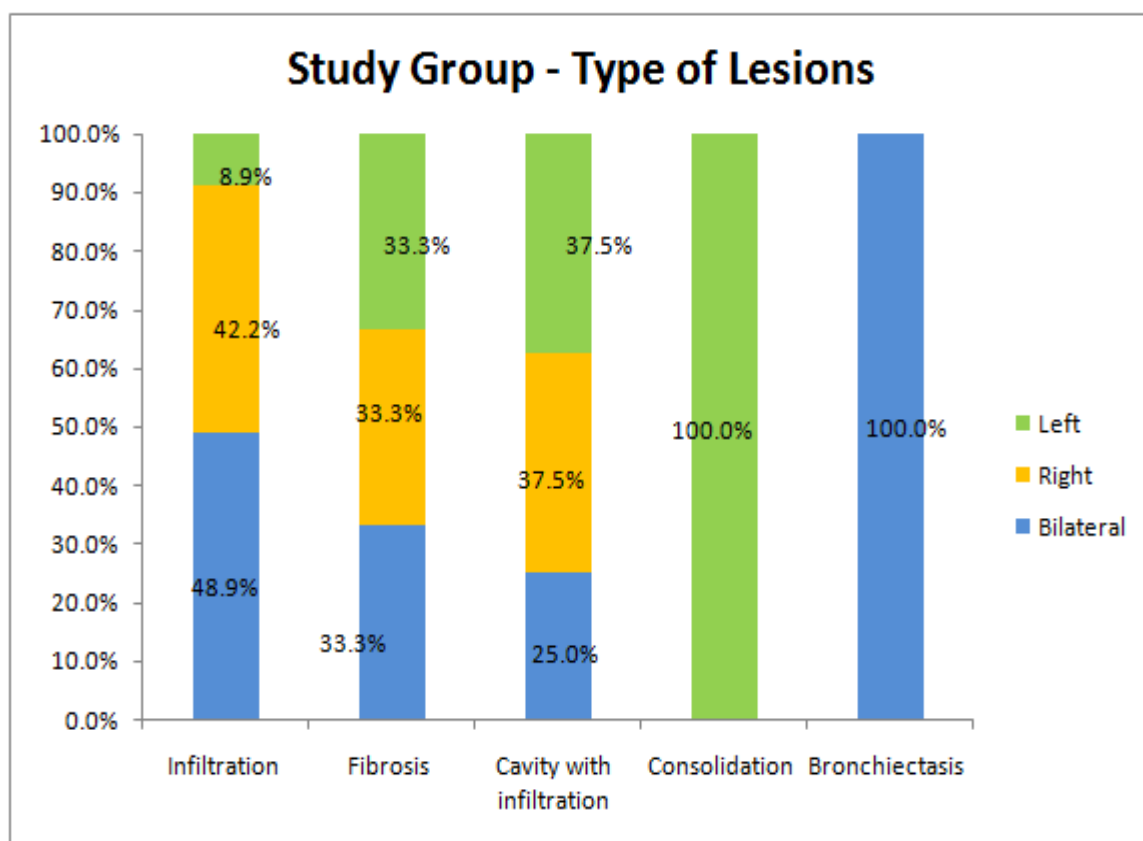
1. This matches a study in Nijmegen, with higher sputum positivity and persistence after treatment owing to the initial higher bacterial load.

8. TYPE OF VARIOUS RADIOLOGICAL LESIONS AND THE PATTERN OF DISTRIBUTION OF SUBJECTS WITH DIABETES AND PT [DM-TB]

[N=56]

TABLE-8A

Type of lesion	Bilatera 1	Right	Left	Bilatera 1	Right	Left
Infiltration	22	19	4	49%	42%	9%
Pleural effusion	0	0	0	0%	0%	0%
Fibrosis	1	1	1	33%	33%	33%
Cavity with infiltration	2	3	3	25%	38%	38%
Consolidation	0	0	1	0%	0%	100%
Bronchiectasis	2	0	0	100%	0%	0%
Infiltration & Cavity with infiltration & Fibrosis	0	0	0	0%	0%	0%
TOTAL	48.2%	16.07%	41.07%			



INFERENCE

In the DM TB GROUP, n=56 the types of lesions were

1. Infiltration in 35 patients
2. pleural effusion in 0 patients
3. fibrosis in 3 patients
4. consolidation in 1 patient
5. bronchiectasis in 2 patients
6. infiltration with cavity in 8 patients

There were more bilateral involvement in the infiltration pattern of lesions and bronchiectasis. Left sided lesions were more with consolidation, cavity with infiltration and fibrosis.

This is in similarity with various studies like,

1. “Tuberculosis had more pronounced radiological signs.”

Lalit Kant., Ind. J . of Tub., No.4., Vol .50 .,New Delhi.,Oct.2003

2. Mboussa et al., Course of TB.,Rev Pneumol clinic .2003.

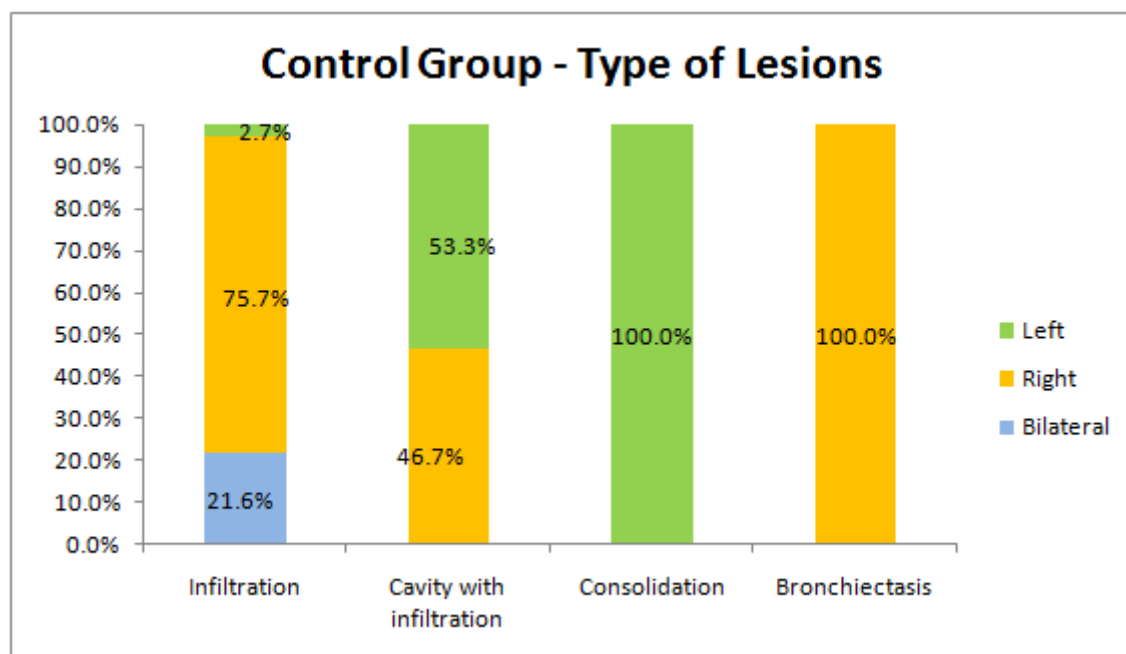
8B. TYPE OF VARIOUS RADIOLOGICAL LESIONS AND THE PATTERN OF DISTRIBUTION AMONG NON DAIBETIC TB POPULATION [NON DM-TB]

[N=56]

TABLE 8 B

Type of lesion	Bilatera l	Right	Left	Bilatera l	Right	Left
Infiltration	8	28	1	22%	76%	3%
Pleural effusion	0	0	0	0%	0%	0%
Fibrosis	0	0	0	0%	0%	0%
Cavity with infiltration	0	7	8	0%	47%	53%
Consolidation	0	0	1	0%	0%	100%
Bronchiectasis	0	1	0	0%	100%	0%
Infiltration & Cavity with infiltration & Fibrosis	0	0	0	0%	0%	0%
	14.2%	64.28%	17.85%			

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INFERENCE

In the NON DM –TB group the following pattern of distribution of radiological lesions were seen.

1. infiltration was seen in 42 patients
2. consolidation was seen in one patient
3. bronchiectasis was seen in one patient
4. Infiltration with cavity was seen in 15 patients.

The study shows a more right sided pattern of infiltration in NON DM –TB Group. Also right sided lesions were seen as equally as left sided lesion in cavity with infiltration type of lesions.

On comparing between the pattern of distribution among DM-TB and NON DM-TB group, there was significant frequency of more bilateral lesions in

TB-DM group.

Also cavity with infiltration were seen bilaterally only DM-TB group. No cases of bilateral cavity with infiltration was seen in NON DM-TB group.

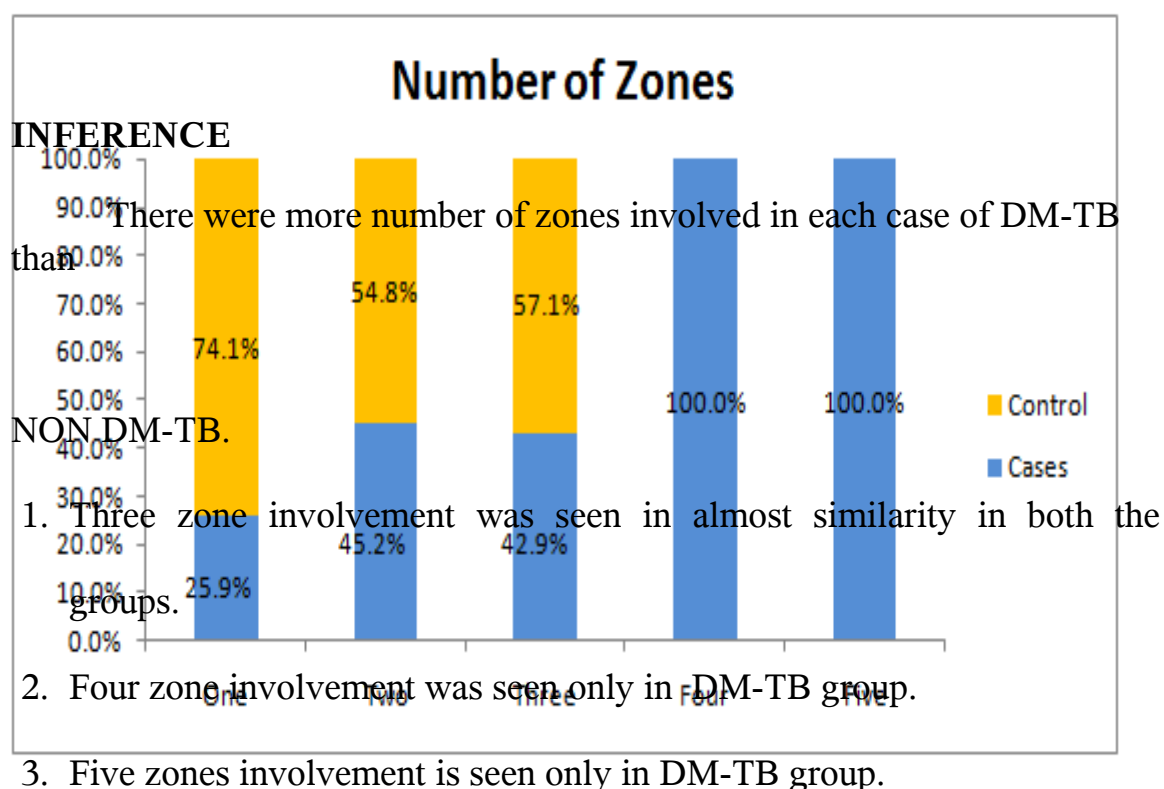
This is in similarity with the other studies like

1. Quazi et al study conducted during 2006, where “bilateral lesions were found in 27% of DM-TB”.
2. Ind. J .Med .res., July 2009.,Young et al., “ concomitant TB and DM is associated with more severe features including increased lung cavitations.”

**9. NO .OF ZONES INVOLV ED IN DM-TB GROUP AND
NON DM - TB GROUP**

TABLE 9

NO.OF ZONES	Cases	Control	Cases	Control
ONE	14	40	26%	74%
TWO	28	34	45%	55%
THREE	6	8	43%	57%
FOUR	2	0	100%	0%
FIVE	1	0	100%	0%
SIX	0	0	0%	0%



This was seen in other related studies like

1. Perz Guzman et al .,Mexico.,2002.,
2. Shaik M.A.et al., Saudi Arabia., 1994., “48% had lower lung zones involved”
3. F.A. Deshmukh ., et al., Bihar 1984.
4. Quazi et al., 2006 Pakistan., “ in 75 x ray films 22 cases showed multiple shadows and atypical radiological involvement with 13% middle zone involved and 58% lower zone involved .”

CONCLUSIONS

The following are the conclusions drawn from the above study of Patients with study of patients with diabetes and pulmonary tuberculosis.

1. The prevalence of pulmonary tuberculosis in diabetics is 11.2 percent.
2. The female and male sex ratio of pulmonary tuberculosis in diabetics is

$$M : F = 1.67 \text{ for study group } \&$$

$$M:F = 3.31 \text{ for control group.}$$
3. Age group distribution of patients suffering from PT and diabetes show a majority (82.1%) belonging to more than 40 years of age control group 62.5%.

In comparison, the control group show a more or less uniform distribution of patients in age groups between 30 to 70 years.

Even then there was no statistical correlation to suggest that diabetes produces more TB lesions in the elderly population. (P = 0.29)

4. Majority of patients in Study group presented with fever

(53.65 %),

chest pain (5.42%), loss of appetite (23.2 %),
weight loss (23.2 %), and Haemoptysis (32.1%) .

In the control group (75%) had fever, 0 % had
chest pain , loss of appetite was seen in 30.4% . Weight loss in
21.4% ,and Haemoptysis in 7.1% .

The symptom complex as per the study
in both group , was found to be similar and there is no statistical
correlation between presence or absence of diabetes influencing
the complaints of the patients .

5. There increased susceptibility of tuberculosis in diabetic
smokers than non smokers

6.Study group:

Radiological studies showed that 48.21% had bilateral
lesions . 16.07% left sided and 41.07 % right sided
lesions.

Control group:

Bilateral 14.2%

Right sided 64.28%

Left sided 17.85%

7. In study group sputum positive were 55.4%

In control group sputum positive were 44.6%

8. In the study group 58.9% were smokers and in
control group 41.1% were smokers.

9. in the study group three zones were involved in 10.7%

four zones involved in 3.57%

five zones were involved in 1.78 %

whereas in control group it was three zones 14.2%

four zones 0%

five zones 0 %

This shows more number zones involved bilaterally in diabetics
than controls.

BIBLIOGRAPHY

1. Mbyana JC, Gan D, Allogt B, Bakker K, Brown JB, Ramachandran A, et al. IDF Diabetes Atlas, 3rd ed. Brussels: Hoorens; 2006
2. Ramachandran A, Snehalatha C, Vijay V. Temporal changes in prevalence of type 2 diabetes and impaired glucose tolerance in urban southern India. *Diabetes Res Clin Pract* 2002; 58: 55-60.
3. King H, Aubert RE, Herman WH. Global Burden of Diabetes, 1995-2025: Prevalence, numerical estimates, and projections. *Diabetes Care* 1998; 21 : 1414-31.
4. World Health Organization. India: Core Programme Clusters, Communicable Diseases and disease Surveillance, Tuberculosis. Geneva: WHO; 2009.
5. World Health Organization: Global Tuberculosis Control WHO Report. Geneva: WHO; 2009.
6. Morton R, editor. *Phthisiolgia: or a treatise of consumptions*. London: Smith and Walford; 1694.
7. Ramadoss A: TB INDIA 2009 RNTCP Status Report 'I am Stopping TB'. (Central TB Division), New Delhi: Ministry of Health and Family Welfare; 2009.
8. Ezung T, Devi NT, Singh NT, Singh TB. Pulmonary tuberculosis and diabetes mellitus-a study. *J Indian Med Assoc* 2002; 100:378-9
9. Patel JC. Complication in 8793 cases of diabetes mellitus 14 year study in Bombay Hospital. *Indian J Med Sci* 1989; 43 : 177-83.
10. Jeon C, Murray M. Diabetes mellitus increase the risk of active tuberculosis: A systematic review of 13 observational studies. *PLoS Med* 2008; 5 : e152.

11. Stevenson CR, Critchley JA, Forouhi NG, Roglic G, Williams BG, Dye C, et al. Diabetes and the risk of tuberculosis : a neglected threat to public health ? *chronic Illn* 2007; 3 : 228-45.
12. Stevenson CR, Forouhi NG, Roglic G, Williams BG, Lauer JA, Dye C, et al. Diabetes and tuberculosis incidence. *BMC Public Health* 2007; 7: 234.
13. Englebach K. Passagerer Diabetes Mellitus bei 2 Tuberkulosekranken. [Transitory Diabetes mellitus in two tuberculotics] *J Beitr Klin Tuberk Spezif Tuberkuloseforsch* 1954;110:470-3.
14. Nichols GP. Diabetes among young tuberculous patients; a review of the association of the two diseases, *Am Rev Tuberc* 1957;76:1016-30.
15. Mugusi F, swai A, Alberti K, Melarty G. increased prevalence of diabetes mellitus in patients with pulmonary tuberculosis in Tanzania. *Tubercle* 1990;71:271-6.
16. Mboussa J, Monabeka H, Kombo M, Yokolo D, Yoka-Mbio A, Yala F. Course of tuberculosis in diabetics. *Rev Pneumol Clin* 2003;59:39-44.
17. Joint Formulary Committee, British National Formulary, British Medical Association, Royal Pharamaceutical Society of Great Britain. British National Formulary. London: BMJ and RPS;2008.
18. Takasu N, Yamada T, Miura H, Sakamoto S, Korenaga M, Nakajima K. et al. Rifampicin- induced early phase hyperglycemia in humans. *Am Rev Respir Dis* 1982;125:23-7.
19. Geerlings SE, Hoepelman AI. Immune dysfunction in patients with diabetes mellitus (DM). *FEMS Immunol Med Microbiol* 1999;26:259-65.
20. Tsukaguchi K, Yoneda T, Yoshikawa M. Case study of interleukin-1 beta, tumor necrosis factor alpha and interleukin-6 production by periphral blood monocytes in patients with diabetes mellitus complicated by pulmonary tuberculosis. *Kekkaku* 1992;67:755-60.

21. Rayfield EJ, Ault MJ, Keusch GT, Brothers MJ, Nechemias C, Smith H, Infection and diabetes: the case for glucose control, *Am J Med* 1982; 72:439-50
22. Pickup JC. Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes. *Diabetes Care* 2004; 27:813-23.
23. Fielder JF, Chaulk CP, Dalvi M, Gachuhi R, Comstock GW, Sterling TR, A high tuberculosis case-fatality rate in a setting of effective tuberculosis control: implications for acceptable treatment success rates. *Int J Tuberc Lung Dis* 2002;6:1114-7.
24. Patel JC, De Souza C, Jigini SS. Diabetes and tuberculosis. *Indian J Tuberc* 1977;24:155-8.
25. Singla R, Osama MM, Khan N, Al-Sharif N, Al-Sayegh MO, Shaikh MA. Factor predicting persistent sputum smear positivity among pulmonary tuberculosis patient 2 months after treatment. *Int J Tuberc Lung Dis* 2003;7:58-64.
26. sosman MC , steidl JH Diabetic tuberculosis . *AM J Roentgenol* 1927 ;17;625-35.
27. Alisijahbana B, sahiratmadja E, Nelwan EJ, Purwa AM, Ahmad Y, Ottenhoff TH, et al. The Effect of type 2 diabetes mellitus on the presentation and treatment response of pulmonary tuberculosis *Clin Infect Dis* 2007;45:428- 35.
28. Fisher-Hoch SP, Whitney E, McCormick JB, Crespo JG, Smith B, Perez AP, et al. type 2 diabetes and multidrug- resistant tuberculosis. *Scand J Infect Dis* 2008;40: 888 -93.
29. Singla R, Khan N, Al- Sharif N, Al- Sayegh MO, Shaikh MA, Osman MM, Influence of diabetes on manifestations and treatment outcome of pulmonary tuberculosis.
30. Suarez-Garcia I, Radriguez-Blanco A, Vidal - Perez JL , Garcia-Viejo ML, Lopez OJ et al., Jaras- ernandez Mj, Lopez OJ., et al. Risk factors for MDR TB in a TB unit IN MADRID., SPAIN.
31. Nijland HM , Rulsamy R , Stalenhoef JE, Nelwan EJ, Alisjabana B.,

et al . Exposure to rifampicin is strongly reduced inpatients with tuberculosis and type 2 diabetes.

32. Balasubramania R., Ramanathan U, Thyagarajan K, Ramachandran, Rajaram K., Indian J of TB., 2007., 54: 168-76
33. Rekha B, Balasubramanian R, Swaminathan S., Ramachandran R, et al., sputum conversion at the end of in treatment of TB with diabetes.